



SEQUENCE LISTING

<110> Ingham et al.

<120> SCREENING ASSAYS FOR HEDGEHOG AGONISTS AND ANTAGONISTS

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<140> 09/711724

<141> 2000-11-13

<150> 08/674509

<151> 1996-07-07

<160> 55

<170> PatentIn version 3.1

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Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
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Val Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu
 225 230 235 240

Thr Phe Leu Asp Arg Asp Glu Gly Ala Lys Lys Val Phe Tyr Val Ile
 245 250 255

Glu Thr Leu Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu
 260 265 270

Leu Phe Val Ala Pro His Asn Asp Ser Gly Pro Thr Pro Gly Pro Ser
 275 280 285

Ala Leu Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val
 290 295 300

Ala Glu Arg Gly Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser
 305 310 315 320

Val Thr Leu Arg Glu Glu Glu Ala Gly Ala Tyr Ala Pro Leu Thr Ala
 325 330 335

His Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val
 340 345 350

Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu
 355 360 365

Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly
 370 375 380

Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly
 385 390 395 400

Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His
 405 410 415

Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
 420 425 430

Ala Val Lys Ser Ser
 435

<210> 12
 <211> 418
 <212> PRT
 <213> Danio rerio

<400> 12

Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser
 1 5 10 15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
 20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
 35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
 50 55 60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
 85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
 100 105 110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
 115 120 125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
 130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
 145 150 155 160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
 165 170 175

```

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
180                               185                               190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
195                               200                               205

Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
210                               215                               220

Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met
225                               230                               235                               240

Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu
245                               250                               255

Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu
260                               265                               270

Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala
275                               280                               285

Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp
290                               295                               300

Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu
305                               310                               315                               320

Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val
325                               330                               335

Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu
340                               345                               350

Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser
355                               360                               365

Phe Leu Phe Pro Gln Asn Ser Ser Ser Arg Ser Asn Ala Thr Leu Gln
370                               375                               380

Gln Glu Gly Val His Trp Tyr Ser Arg Leu Leu Tyr Gln Met Gly Thr
385                               390                               395                               400

Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn
405                               410                               415

```

Ser Ser

<210> 13
 <211> 462
 <212> PRT
 <213> Homo sapiens

<400> 13

Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu
 1 5 10 15

Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
 20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
 35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
 50 55 60

Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
 85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser
 100 105 110

Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
 115 120 125

Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg
 130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met
 145 150 155 160

Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
 165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
 180 185 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu Glu
 195 200 205

Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val
 210 215 220

Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu Thr
 225 230 235 240

Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu
 245 250 255

Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu
 260 265 270

Phe Val Ala Pro His Asn Asp Ser Ala Thr Gly Glu Pro Glu Ala Ser
 275 280 285

Ser Gly Ser Gly Pro Pro Ser Gly Gly Ala Leu Gly Pro Arg Ala Leu
 290 295 300

Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu
 305 310 315 320

Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr
 325 330 335

Leu Ser Glu Glu Ala Ala Gly Ala Tyr Ala Pro Leu Thr Ala Gln Gly
 340 345 350

Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu
 355 360 365

Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His
 370 375 380

Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp
 385 390 395 400

Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr
 405 410 415

Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile
 420 425 430

His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp
 435 440 445

Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser
 450 455 460

<210> 14
 <211> 312
 <212> PRT
 <213> Homo sapiens

<400> 14

Arg Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu Ala
 1 5 10 15

Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu
 20 25 30

Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu
 35 40 45

Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr
 50 55 60

Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr
 65 70 75 80

Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser Glu His Ser
 85 90 95

Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala Gln Val Arg
 100 105 110

Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg Pro Gly Asp
 115 120 125

Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe Ser Asp Val
 130 135 140

Leu Ile Leu Leu Asp Arg Glu Pro His Arg Leu Arg Ala Phe Gln Val
 145 150 155 160

Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr Pro Ala His
 165 170 175

Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala Arg Phe Arg
 180 185 190

Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val Leu Val Ala
 195 200 205

Gly Ala Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val Ser Thr His
 210 215 220

Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly Thr Leu Val
 225 230 235 240

Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala Asp His His
 245 250 255

Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His Ser Leu Ala
 260 265 270

Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr Pro Gln Leu
 275 280 285

Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser Phe His Pro
 290 295 300

Leu Gly Met Ser Gly Ala Gly Ser
 305 310

<210> 15
 <211> 64
 <212> PRT
 <213> Danio rerio

<400> 15

Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn
 1 5 10 15

His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp
 20 25 30

Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp
 35 40 45

Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr Leu Ser Arg
 50 55 60

<210> 16
 <211> 64
 <212> PRT
 <213> Danio rerio

<400> 16

Gln Arg Cys Lys Glu Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn
 1 5 10 15

Met Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp
 20 25 30

Gly Asn His Phe Glu Asp Ser Leu His Tyr Glu Gly Arg Ala Val Asp
 35 40 45

Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly Met Phe Ala Arg
 50 55 60

<210> 17
 <211> 64
 <212> PRT
 <213> Danio rerio

<220>
 <221> MISC_FEATURE
 <222> (1)..(221)
 <223> Xaa=unknown amino acid

<400> 17

Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn
 1 5 10 15

Leu Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp
 20 25 30

Gly Leu His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp
 35 40 45

Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Arg Met Leu Ala Arg
 50 55 60

<210> 18
 <211> 38
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Degenerate oligonucleotide
 <220>

<220>
 <221> misc_feature
 <222> (1)..(36)
 <223> n=inosine

<400> 18
 ggaattccca gcagntgcta aaggaagcaa gngctnaa

38

<210> 19
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Degenerate oligonucleotide

<220>
 <221> misc_feature
 <222> (1)..(33)
 <223> n=inosine

<400> 19
 tcatcgatgg acccagatcg aaanccngct ctc

33

<210> 20
 <211> 29
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Degenerate oligonucleotide

<220>
 <221> misc_feature
 <222> (1)..(27)
 <223> n=inosine

<400> 20
 gctctagagc tcnacngcna gancgtngc

29

<210> 21
 <211> 50
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Annealed oligonucleotide lac1

<400> 21
 agctgtcgac gcggccgcta cgtaggttac cgacgtcaag cttagatctc

50

<210> 22
 <211> 50
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Annealed oligonucleotide lac2

<400> 22
 agctgagatc taagcttgac gtcggtaacc tacgtagcgg ccgcgtcgac

50

<210> 23
 <211> 45
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Sf-1 oligonucleotide

 <400> 23
 gatcggccag gcaggcctcg cgatatcgtc accgcggtat tcgaa 45

 <210> 24
 <211> 30
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Sf-2 oligonucleotide

 <400> 24
 agtgccagtc ggggccccca gggccgcgcc 30

 <210> 25
 <211> 20
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Oligonucleotide 137

 <400> 25
 taccacagcg gatggttcgg 20

 <210> 26
 <211> 20
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Oligonucleotide 138

 <400> 26
 gtggtggtta tgccgatcgc 20

 <210> 27
 <211> 21
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Oligonucleotide WPR2

 <400> 27
 taagaggcct ataagaggcg g 21

 <210> 28
 <211> 20
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Oligonucleotide 924

 <400> 28

aagtcagccc agaggagact

20

<210> 29

<211> 6

<212> PRT

<213> Mus musculus

<400> 29

Cys Gly Pro Gly Arg Gly

1

5

<210> 30

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide hh5.1

<220>

<221> misc_feature

<222> (1)..(29)

<223> n=inosine

<400> 30

agcagntgct aaaggaagca agngctnaa

29

<210> 31

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide hh3.3

<220>

<221> misc_feature

<222> (1)..(23)

<223> n=inosine

<400> 31

ctcnacngcn aganckgtng cna

23

<210> 32

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide to amplify Shh ORF

<400> 32

ctgcagggat ccacatgacg gcttttgacg ag

32

<210> 33

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide to amplify Shh ORF

<400> 33

ctgcagggat ccttattcca cacgagggat t

31

<210> 34

<211> 471

<212> PRT

<213> Drosophila melanogaster

<400> 34

Met	Asp	Asn	His	Ser	Ser	Val	Pro	Trp	Ala	Ser	Ala	Ala	Ser	Val	Thr
1				5					10					15	

Cys	Leu	Ser	Leu	Gly	Cys	Gln	Met	Pro	Gln	Phe	Gln	Phe	Gln	Phe	Gln
			20					25					30		

Leu	Gln	Ile	Arg	Ser	Glu	Leu	His	Leu	Arg	Lys	Pro	Ala	Arg	Arg	Thr
		35					40					45			

Gln	Thr	Met	Arg	His	Ile	Ala	His	Thr	Gln	Arg	Cys	Leu	Ser	Arg	Leu
	50					55					60				

Thr	Ser	Leu	Val	Ala	Leu	Leu	Leu	Ile	Val	Leu	Pro	Met	Val	Phe	Ser
65					70					75					80

Pro	Ala	His	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Leu	Gly	Arg	His	Arg	Ala
				85					90					95	

Arg	Asn	Leu	Tyr	Pro	Leu	Val	Leu	Lys	Gln	Thr	Ile	Pro	Asn	Leu	Ser
		100						105					110		

Glu	Tyr	Thr	Asn	Ser	Ala	Ser	Gly	Pro	Leu	Glu	Gly	Val	Ile	Arg	Arg
		115					120					125			

Asp	Ser	Pro	Lys	Phe	Lys	Asp	Leu	Val	Pro	Asn	Tyr	Asn	Arg	Asp	Ile
	130					135					140				

Leu	Phe	Arg	Asp	Glu	Glu	Gly	Thr	Gly	Ala	Asp	Gly	Leu	Met	Ser	Lys
145					150					155					160

Arg	Cys	Lys	Glu	Lys	Leu	Asn	Val	Leu	Ala	Tyr	Ser	Val	Met	Asn	Glu
				165					170					175	

Trp	Pro	Gly	Ile	Arg	Leu	Leu	Val	Thr	Glu	Ser	Trp	Asp	Glu	Asp	Tyr
			180					185					190		

His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
195 200 205

Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
210 215 220

Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His
225 230 235 240

Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His
245 250 255

Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg
260 265 270

Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr
275 280 285

Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg
290 295 300

Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly
305 310 315 320

Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro
325 330 335

Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys
340 345 350

Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln
355 360 365

Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro
370 375 380

Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys
385 390 395 400

Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro
405 410 415

Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln
420 425 430

Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly
 435 440 445

Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu
 450 455 460

Pro Gln Ser Trp Arg His Asp
 465 470

<210> 35
 <211> 73
 <212> PRT
 <213> Gallus gallus

<400> 35

Arg Cys Lys Glu Arg Val Asn Ser Leu Ala Ile Ala Val Met His Met
 1 5 10 15

Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly
 20 25 30

His His Leu Pro Asp Ser Leu His Tyr Glu Gly Arg Ala Leu Asp Ile
 35 40 45

Thr Thr Ser Asp Arg Asp Arg His Lys Tyr Gly Met Leu Ala Arg Leu
 50 55 60

Ala Val Glu Ala Gly Phe Asp Trp Val
 65 70

<210> 36
 <211> 73
 <212> PRT
 <213> Gallus gallus

<400> 36

Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln
 1 5 10 15

Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly
 20 25 30

His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile
 35 40 45

Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu
 50 55 60

Ala Val Glu Ala Gly Phe Asp Trp Val
65 70

<210> 37
<211> 64
<212> PRT
<213> Danio rerio

<400> 37

Lys Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn
1 5 10 15

Glu Trp Pro Gly Ile Arg Leu Val Val Thr Glu Ser Trp Asp Glu Asp
20 25 30

Tyr His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr
35 40 45

Ile Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg
50 55 60

<210> 38
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Degenerate primer

<220>
<221> misc_feature
<222> (1)..(28)
<223> n=inosine

<400> 38
aaaagcttta ytgtyaygtn ggnathgg

28

<210> 39
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Degenerate primer

<220>
<221> misc_feature
<222> (1)..(28)
<223> n=inosine

<400> 39
aagaattcta ngcrttrtar ttrttngg

28

<210> 40

<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Degenerate Shh
polypeptide general formula

<220>
<221> SITE
<222> (7)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Phe, Tyr, or Trp

<220>
<221> SITE
<222> (9)
<223> Xaa=Arg, His or Lys

<220>
<221> SITE
<222> (44)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser. or Thr

<220>
<221> SITE
<222> (85)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
<221> SITE
<222> (93)
<223> Xaa=Lys, Arg, His, Asn, or Gln

<220>
<221> SITE
<222> (98)
<223> Xaa=Lys, Arg or His

<220>
<221> SITE
<222> (112)
<223> Xaa=Ser, Thr, Tyr, Trp, or Phe

<220>
<221> SITE
<222> (132)
<223> Xaa=Lys, Arg or His

<220>
<221> SITE
<222> (137)
<223> Xaa=Met, Cys, Ser, or Thr

<220>
<221> SITE
<222> (139)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
<221> SITE

<222> (181)
<223> Xaa=Leu, Val, Met, Thr, or Ser

<220>
<221> SITE
<222> (183)
<223> Xaa=His, Phe, Tyr, Ser, Thr, Met, or Cys

<220>
<221> SITE
<222> (185)
<223> Xaa=Gln, Asn, Glu, or Asp

<220>
<221> SITE
<222> (186)
<223> Xaa=His, Phe, Tyr, Thr, Gln, Asn, Glu, or Asp

<220>
<221> SITE
<222> (189)
<223> Xaa=Gln, Asn, Glu, Asp, Thr, Ser, Met, or Cys

<220>
<221> SITE
<222> (191)
<223> Xaa=Ala, Gly, Cys, Leu, Val, or Met

<220>
<221> SITE
<222> (196)
<223> Xaa=Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser,
Thr, or Cys

<220>
<221> SITE
<222> (200)
<223> Xaa=Arg, Lys, Met, or Ile

<220>
<221> SITE
<222> (206)
<223> Xaa=Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr,
or Met

<220>
<221> SITE
<222> (207)
<223> Xaa=Ala, Gly, Cys, Asp, Asn, Glu, or Gln

<220>
<221> SITE
<222> (209)
<223> Xaa=Arg, Lys, Met, Ile, Asn, Asp, or Glu

<220>
<221> SITE
<222> (211)
<223> Xaa=Leu, Val, Met, or Ile

<220>
 <221> SITE
 <222> (212)
 <223> Xaa=Phe, Tyr, Thr, His, or Trp

<220>
 <221> SITE
 <222> (216)
 <223> Xaa=Ile, Val, Leu, or Met

<220>
 <221> SITE
 <222> (217)
 <223> Xaa=Met, Cys, Ile, Leu, Val, Thr, or Ser

<220>
 <221> SITE
 <222> (219)
 <223> Xaa=Leu, Val, Met, Thr, or Ser

<400> 40
 Cys Gly Pro Gly Arg Gly Xaa Gly Xaa Arg Arg His Pro Lys Lys Leu
 1 5 10 15
 Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30
 Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Xaa Arg Asn Ser Glu
 35 40 45
 Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
 50 55 60
 Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
 65 70 75 80
 Asp Lys Leu Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp Pro Gly
 85 90 95
 Val Xaa Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Xaa
 100 105 110
 Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
 115 120 125
 Asp Arg Asp Xaa Ser Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala Val Glu
 130 135 140
 Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
 145 150 155 160
 Ser Val Lys Ala Glu Asn Ser Val Ala Ala Lys Ser Gly Gly Cys Phe
 165 170 175
 Pro Gly Ser Ala Xaa Val Xaa Leu Xaa Xaa Gly Gly Xaa Lys Xaa Val
 180 185 190
 Lys Asp Leu Xaa Pro Gly Asp Xaa Val Leu Ala Ala Asp Xaa Xaa Gly
 195 200 205

Xaa Leu Xaa Xaa Ser Asp Phe Xaa Xaa Phe Xaa Asp Arg
 210 215 220

<210> 41
 <211> 167
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Degenerate
 hedgehog polypeptide general formula

<220>
 <221> SITE
 <222> (7)
 <223> Xaa=Gly, Ala, Val, Leu, Ile, Pro, Phe, or Tyr

<220>
 <221> SITE
 <222> (8)
 <223> Xaa=Gly, Ala, Val, Leu, or Ile

<220>
 <221> SITE
 <222> (9)
 <223> Xaa=Gly, Ala, Val, Leu, Ile, Lys, His, or Arg

<220>
 <221> SITE
 <222> (12)
 <223> Xaa=Lys, Arg or His

<220>
 <221> SITE
 <222> (13)
 <223> Xaa=Phe, Trp or Tyr or an amino acid gap

<220>
 <221> SITE
 <222> (14)
 <223> Xaa=Gly, Ala, Val, Leu, or Ile or an amino acid
 gap

<220>
 <221> SITE
 <222> (17)
 <223> Xaa=Asn, Gln, His, Arg, or Lys

<220>
 <221> SITE
 <222> (19)
 <223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
 <221> SITE
 <222> (22)
 <223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
 <221> SITE

<222> (27)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
<221> SITE
<222> (29)
<223> Xaa=Ser, Thr, Gln, or Asn

<220>
<221> SITE
<222> (30)
<223> Xaa=Met, Cys, Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>
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<223> Xaa=Gly, Alka, Val, Leu, Ile, or Pro

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<222> (33)
<223> Xaa=Arg, His or Lys

<220>
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<223> Xaa=Thr or Ser

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<223> Xaa=Arg, His or Lys

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<222> (54)
<223> Xaa=Asp or Glu

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<223> Xaa=Ser or Thr

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<223> Xaa=Met, Cys, Gln, Asn, Arg, Lys, or His

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<223> Xaa=Arg, His or Lys

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<223> Xaa=Trp, Phe, Tyr, Arg, His, or Lys

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<223> Xaa=Asp or Glu

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<223> Xaa=Arg, His or Lys

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, Thr, or Cys

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Thr, or Ser

<220>
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<223> Xaa=Asp or Glu

<400> 41
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Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa	35	40	45
Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile	50	55	60
Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg	65	70	75
Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp	85	90	95
Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His	100	105	110
His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr	115	120	125
Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala	130	135	140
Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa	145	150	155
His Xaa Ser Val Lys Xaa Xaa	165		

<210> 42

<211> 3900

<212> DNA

<213> Homo sapiens

<400> 42

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atagataagg gcaaagcgcg tggcagccgc acggcgatct atctgcgatc agtattccag 180

tcccacctcg aaaccctcgg cagctccgtg caaaagcacg cgggcaaggt gctattcgtg 240

gctatcctgg tgctgagcac cttctgcgtc ggcctgaaga gcgccagat cactccaag 300

gtgcaccagc tgtggatcca ggagggcggc gggctggagg cggaactggc ctacacacag 360

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gccaccgccg tcaaggtgca cctctacgac accgaatggg ggctgcgcga catgtgcaac 540

atgccgagca cgccctcctt cgagggcatc tactacatcg agcagatcct gcgccacctc 600

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<210> 43
<211> 24
<212> DNA
<213> Artificial Sequence

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<220>
<223> primer

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<400> 43
accgagggtg gggacgaaga tggc

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24

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<210> 44

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<211> 25
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 44
 cgctcggtcg tacggcatga acgac

25

<210> 45
 <211> 25
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 45
 atggggatgt gtgtgggtcaa gtgta

25

<210> 46
 <211> 25
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 46
 ttcacagact ctcaaagtgt atttt

25

<210> 47
 <211> 73
 <212> PRT
 <213> Drosophila melanogaster

<400> 47

Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu
 1 5 10 15

Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr
 20 25 30

His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
 35 40 45

Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
 50 55 60

Ala Val Glu Ala Gly Phe Asp Trp Val
 65 70

<210> 48
 <211> 167

<212> PRT
 <213> Mus musculus

<400> 48

Cys Gly Pro Gly Arg Gly Pro Val Gly Arg Arg Arg Tyr Val Arg Lys
 1 5 10 15

Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe Val Pro Ser Met Pro Glu
 20 25 30

Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu Gly Arg Val Thr Arg Gly
 35 40 45

Ser Glu Arg Phe Arg Asp Leu Val Pro Asn Tyr Asn Pro Asp Ile Ile
 50 55 60

Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp Arg Leu Met Thr Glu Arg
 65 70 75 80

Cys Lys Glu Arg Val Asn Ala Leu Ala Ile Ala Val Met Asn Met Trp
 85 90 95

Pro Gly Val Arg Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His
 100 105 110

His Ala Gln Asp Ser Leu His Tyr Glu Gly Arg Ala Leu Asp Ile Thr
 115 120 125

Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala
 130 135 140

Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Arg Asn His Ile
 145 150 155 160

His Val Ser Val Lys Ala Asp
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<210> 49
 <211> 118
 <212> PRT
 <213> Mus musculus

<400> 49

Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe
 1 5 10 15

Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys

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<210> 51
<211> 165
<212> PRT
<213> Homo sapiens
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<400> 51

Cys Gly Pro Gly Arg Gly Phe Gly Lys Arg Arg His Pro Lys Lys Leu
 1 5 10 15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Ser Arg Asn Ser Glu
 35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
 50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
 65 70 75 80

Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly
 85 90 95

Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser
 100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
 115 120 125

Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu
 130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
 145 150 155 160

Ser Val Lys Ala Glu
 165

<210> 52

<211> 165

<212> PRT

<213> Gallus gallus

<400> 52

Cys Gly Pro Gly Arg Gly Ile Gly Lys Arg Arg His Pro Lys Lys Leu
 1 5 10 15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu
 35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
 50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
 65 70 75 80

Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly
 85 90 95

Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser
 100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
 115 120 125

Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu
 130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
 145 150 155 160

Ser Val Lys Ala Glu
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<210> 53
 <211> 165
 <212> PRT
 <213> Mus musculus

<400> 53

Cys Gly Pro Gly Arg Gly Phe Gly Lys Arg Arg His Pro Lys Lys Leu
 1 5 10 15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu
 35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
 50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
 65 70 75 80

Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly
 85 90 95

Val Arg Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser
 100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
 115 120 125

Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu
 130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
 145 150 155 160

Ser Val Lys Ala Glu
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<210> 54

<211> 165

<212> PRT

<213> Danio rerio

<400> 54

Cys Gly Pro Gly Arg Gly Tyr Gly Arg Arg Arg His Pro Lys Lys Leu
 1 5 10 15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu
 35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
 50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
 65 70 75 80

Asp Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn His Trp Pro Gly
 85 90 95

Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Phe
 100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
 115 120 125

Asp Arg Asp Lys Ser Lys Tyr Gly Thr Leu Ser Arg Leu Ala Val Glu
 130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
 145 150 155 160

Ser Val Lys Ala Glu
 165

<210> 55

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> N-terminal exogenous leader

<400> 55

Met Gly Ser Ser His His His His His His Leu Val Pro Arg Gly Ser
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His Met
